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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,436	12/22/2004	Hilde Azjin	TIP0015 US	7541

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	

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06/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,436	AZJIN ET AL.	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2 and 5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 18 April 2008 has been entered.

DETAILED ACTION

This Office Action is in response to the amendment filed 18 April 2008. Claims 1, 3 and 4 have been cancelled. Claims 2 and 5 are pending and currently examined.

Claim 2 is objected to because a hyphen is missing between the words "anti" and "HIV" in the claim language.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 2 and 5 under 35 U.S.C. §112, second paragraph, as being indefinite is **maintained**. Although Applicants' amendment clarifies the HIV strain

that the position 194 is in reference to, the claims do not particularly point out the wild type residue at position 194. Applicants may consider amending the claims to recite "wherein the wild type amino acid glutamate is mutated to glycine (E194G)," as supported by Table I in the specification, to obviate this rejection.

The rejection of claims 2 and 5 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification commensurate in scope is **withdrawn** in response to Applicants' amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 2 and 5 under 35 U.S.C. §103(a) as being obvious over Stein *et al.* (1994, hereinafter "Stein") in view of Servais *et al.* (10 March 2001, GenBank Accession Number CAB 86592, hereinafter "Servais") is withdrawn in response to Applicants' amendment. However, the amendment necessitates the following **new ground of rejection**:

Claims 2 and 5 are rejected under 35 U.S.C. §103(a) as being unpatentable over Stein *et al.* (1994, hereinafter "Stein") in view of Servais *et al.* (10 March 2001, GenBank

Accession Number CAB 86592, hereinafter "Servais") and Kim et al. (2001, hereinafter "Kim").

The instant claims are directed to a method for evaluating the effectiveness of an HIV reverse transcriptase inhibitor (RTI), excluding AZT, as an anti-HIV therapy for a patient infected with at least one mutant HIV strain comprising:

(i) collecting a sample from an HIV-infected patient;

(ii) determining whether the sample comprises a nucleic acid encoding HIV reverse transcriptase having at least one mutation at the position 194, wherein the wild type amino acid is mutated to glycine as compared to the wild-type HIV strain IIIB/LAI;

(iii) introducing said HIV reverse transcriptase inhibitor to said sample containing said mutation;

(iv) comparing the effectiveness of said inhibitor in said samples containing said reverse transcriptase mutation with a sample containing no said mutation; and

(v) correlating the presence of said at least one mutation of step (ii) to a change in effectiveness of said HIV reverse transcriptase inhibitor.

Stein discloses sequence analysis of HIV RT from HIV patients comprising collecting a sample from an HIV-infected patient; determining whether the sample comprises a nucleic acid encoding HIV reverse transcriptase having at least one mutation at position 194; and correlating the presence of the mutation to a change in

effectiveness or susceptibility of azidothymidine (AZT) (page 117, Table II), a nucleoside reverse transcriptase inhibitor (NRTI).

Stein does not disclose the specific amino acid change to glycine (G) at position 194.

Servais discloses a sequence analysis of samples of patients on treatment with two NRTIs, zidovudine and zalcitabine (see the article cited in the Genbank data sheet mailed on 13 March 2006), and the 194G mutation is present in the reverse transcriptase in the sequence submitted to the GenBank under accession number CAB86592.

Stein and Servais do not expressly suggest introducing a RTI to a sample containing the drug-resistant mutation(s).

However, Kim discloses a method of introducing HIV nucleoside reverse transcriptase inhibitor, 3'-fluoro-3'-deoxythymidine (FLT) to both a wild-type HIV-1 isolate and multidrug-resistant HIV-1 patient isolates containing known mutations. The activity of FLT and AZT against the patient isolates are determined by drug susceptibility assays and compared to the activity against the wild-type isolate (Abstract).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the drug-resistance mutation profiles taught by Stein and Servais because both evaluation methods use the same RTI, AZT, and to modify the evaluation method of Stein to further include the steps as suggested by Kim. One having ordinary skill in the art would have been motivated to do this so that the mutation

profile contributes to a more complete and accurate drug evaluation for any novel HIV RTIs while the *in vitro* test of introducing a RTI to a sample containing the known RTI-resistant mutation(s) helps identify more potent RTIs in a rapid assay. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicants' arguments filed 18 April 2008 have been fully considered but they are not persuasive.

Applicants argue that AZT is not a reverse transcriptase inhibitor (RTI) and hence Stein fails to teach a method for evaluating the effectiveness of an HIV reverse transcriptase inhibitor. Examiner respectfully disagrees. It is unclear how Applicants came to the conclusion that AZT is NOT a RTI. Applicants' contention, "the function of AZT is to inhibit the HIV reverse transcription as opposed to the HIV reverse transcriptase" is repugnant to the teachings of the prior art and contradicts their own disclosure in this application. HIV reverse transcriptase is the enzyme required for the process of reverse transcription. A RTI inhibits the enzyme and thereby inhibits the process of reverse transcription. AZT is well known in the art as a nucleoside reverse transcriptase inhibitor (Kim, 2001). AZT is also known as zidovudine, which is disclosed in the specification (page 5, line 34) as one of the reverse transcriptase inhibitors that can be used in the claimed method. Therefore, Stein clearly discloses a method of evaluating the effectiveness of an HIV RTI, such as AZT, by determining whether the

HIV-infected patient sample comprises the mutation at position 194 in the HIV reverse transcriptase. Applicant's arguments with respect to steps (iii)-(v) of claims 2 and 5 have been considered but are moot in view of the new ground of rejection.

Applicants also argue that Servais does not teach reverse transcriptase inhibitors or methods of evaluating a reverse transcriptase inhibitor. Examine does not concur. The publication cited in the Genbank sequence under accession number CAB86592 clearly discloses a sequence analysis of samples of patients on treatment with two RTIs, zidovudine and zalcitabine.

Conclusion

No claim is allowable.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./
Examiner, Art Unit 1648

/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648